PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 63323

Title: Mechanisms involved in selecting and maintaining neuroblastoma cancer stem cell populations, and perspectives for therapeutic targeting

Reviewer's code: 02446263

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Mexico

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-02-01 23:38

Reviewer performed review: 2021-02-12 20:50

Review time: 10 Days and 21 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The review by Farina et al. aimed to describe the characteristics of neuroblastoma CSCs as well as their targeting. The manuscript´s language is, in general, adequate. However, it goes far beyond the scope that the authors defined. Since the authors present evidence unrequired to achieve their goals, the text is too long. The main parts of the manuscripts require serious improvements in cohesion. Most importantly, the authors fail to provide their own perspective of the field since discussion of the presented evidence is almost absent.   Thus, I suggest to modify the manuscript as follows: 1. The first section "The vertebrate neural crest …" contains information reviewed elsewhere. Compress it by: i) quoting relevant reviews; ii) limiting your examples to mammals, and iii) checking that the reader needs the information for understanding the subsequent sections (for example, it is essential to present the info regarding the NCSC). 2. "Neuroblastoma" can also be condensed, making "The cellular origins of …" the first important section. 3. "Molecules and mechanisms…", one of the central parts of the review, has important information but fails to present it in an ordered manner; it is a list of molecules/stimuli/cellular structures and references. You need to organize the chosen examples and make the subsections cohesive. For example, you could put transcription factors together or organize by signaling pathways.   4.   Remove the lncRNA sections, unless you could integrate them with the rest of the info. 5. The last section, "Therapeutic prospects …", also needs extensive restructuring (see points 3 and 4 above). For example, you can join the CAR T-cells section with "markers" since the cytotoxic cells aim to recognize CSC surface markers. "Nanoparticles" is not a targeting strategy, but a delivery strategy, and thus the info can be relocated in relevant sections. After deciding what the new order will be, generate a self-explanative figure that condenses the information.   6. Review carefully gene and protein nomenclature along the manuscript. 7. Discuss the evidence

presented and point what is still to be addressed. The lack of discussion is one the main flaws of this review.

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 63323

Title: Mechanisms involved in selecting and maintaining neuroblastoma cancer stem cell populations, and perspectives for therapeutic targeting

Reviewer's code: 02842279

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor, Surgeon

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-01-28 23:39

Reviewer performed review: 2021-02-14 15:29

Review time: 16 Days and 15 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this review, the authors carefully summarized that origin of neuroblastoma (NB) and the relationship of NB progression of cancer stem cell (CSC)-like subpopulations. The authors provided a comprehensive review of the salient molecules, signalling pathways, mechanisms, tumor microenvironmental and therapeutic conditions involved in promoting, selecting and maintaining NB CSC subpopulations, and that underpin their therapy-resistant, self-renewing metastatic behaviour. Finally, they reviewed potential therapeutic strategies and future prospects for targeting and eradication these bastions of NB therapeutic resistance, post-therapeutic relapse and metastatic progression. The authors reviewed all aspects in detail. However, the content, especially the basic aspects, should be more concise.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Stem Cells

Manuscript NO: 63323

Title: Mechanisms involved in selecting and maintaining neuroblastoma cancer stem cell populations, and perspectives for therapeutic targeting

Reviewer's code: 02842279

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor, Surgeon

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-01-27

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2021-03-12 03:09

Reviewer performed review: 2021-03-12 03:24

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have addressed my questions in the response and in the revised manuscript. All details in the last comments have been mentioned and corresponding changes have been made. I have no further comments for this latest version.